

=> fil reg

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 SEP 2004 HIGHEST RN 739335-06-9

DICTIONARY FILE UPDATES: 3 SEP 2004 HIGHEST RN 739335-06-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

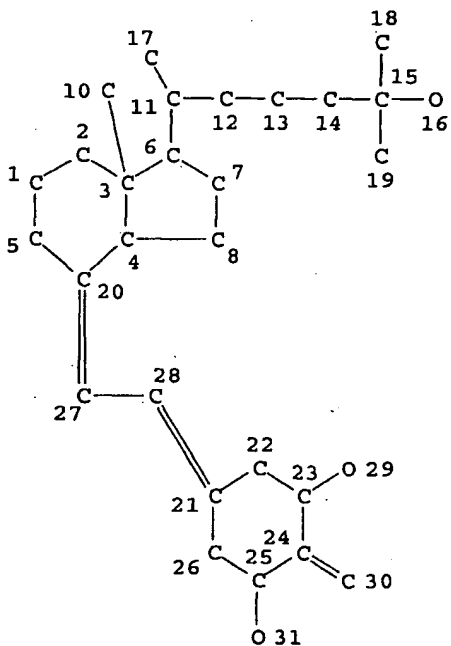
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que l18

L16 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS 'ATOM'

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L18 3 SEA FILE=REGISTRY FAM FUL L16

100.0% PROCESSED 15 ITERATIONS  
SEARCH TIME: 00.00.01

3 ANSWERS

=> d his

(FILE 'HOME' ENTERED AT 13:40:41 ON 05 SEP 2004)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:41:00 ON 05 SEP 2004

E PLUM L/AU  
L1 22 S E3,E4,E6,E7  
E CLAGETTE M/AU  
L2 1 S E2  
E CLAGETTE D/AU  
E DAME M/AU  
L3 12 S E3,E4,E6-E8  
E DELUCA H/AU  
L4 1160 S E3,E6-E10  
E DE LUCA H/AU  
L5 38 S E5,E6  
L6 1213 S L1-L5

FILE 'REGISTRY' ENTERED AT 13:42:24 ON 05 SEP 2004

FILE 'HCAPLUS' ENTERED AT 13:42:24 ON 05 SEP 2004

SET SMARTSELECT ON  
L7 SEL L6 1- RN : 2546 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 13:43:02 ON 05 SEP 2004

L8 2546 S L7  
L9 729 S L8 AND C6/ES AND C5-C6/ES AND 3/NR  
L10 294 S L9 AND 3/O  
L11 92 S L10 AND 27/C  
L12 54 S L11 AND 44/H  
L13 23 S L12 AND 1 3 25 TRIOL  
L14 2 S L13 AND 2 METHYLENE  
L15 52 S L12 NOT L14  
L16 STR  
L17 0 S L16 FAM SAM  
L18 3 S L16 FAM FUL  
SAV L18 QAZI782/A  
L19 3 S L14,L18

FILE 'HCAOLD' ENTERED AT 13:48:18 ON 05 SEP 2004

L20 0 S L18

FILE 'HCAPLUS' ENTERED AT 13:48:23 ON 05 SEP 2004

L21 22 S L18  
L22 19 S L21 AND L6  
L23 3 S L21 NOT L22  
L24 22 S L21-L23  
L25 0 S L24 AND LIFE(L) EXPECT?  
L26 0 S L24 AND LONGEV?  
E LONGEVITY/CT  
E E3+ALL  
L27 1 S L24 AND E3+OLD,NT,PFT,RT  
L28 22 S L24,L27

FILE 'USPATFULL, USPAT2' ENTERED AT 13:50:06 ON 05 SEP 2004

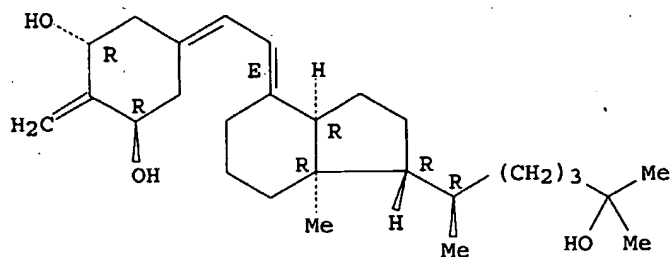
L29 24 S L18

FILE 'REGISTRY' ENTERED AT 13:50:22 ON 05 SEP 2004

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L18 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 235108-14-2 REGISTRY  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E,14 $\beta$ )- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C27 H44 O3  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
 DT.CA Caplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

Absolute stereochemistry.  
 Double bond geometry as shown.



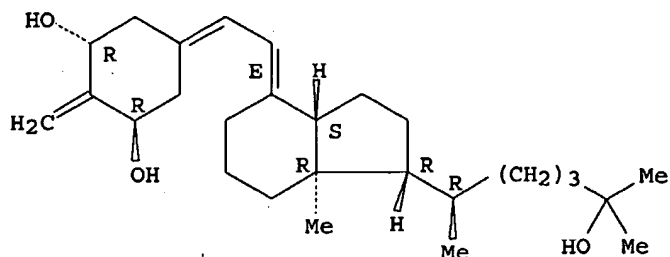
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:144749

L18 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 213319-29-0 REGISTRY  
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
 (1 $\alpha$ ,3 $\beta$ ,7E)- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-  
 FS STEREOSEARCH  
 MF C27 H44 O3  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL  
 DT.CA Caplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10 REFERENCES IN FILE CA (1907 TO DATE)

11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:247113

REFERENCE 2: 139:271426

REFERENCE 3: 136:401925

REFERENCE 4: 136:112696

REFERENCE 5: 135:358086

REFERENCE 6: 135:304063

REFERENCE 7: 135:288953

REFERENCE 8: 133:267021

REFERENCE 9: 130:52625

REFERENCE 10: 129:245332

L18 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN

RN 213250-70-5 REGISTRY

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1α,3β,7E,20S)-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-

FS STEREOSEARCH

MF C27 H44 O3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

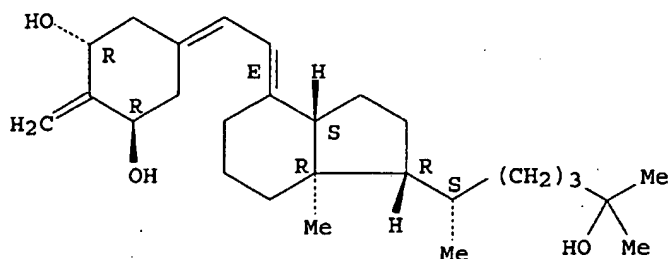
DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

15 REFERENCES IN FILE CA (1907 TO DATE)  
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:386155  
REFERENCE 2: 140:13126  
REFERENCE 3: 139:317525  
REFERENCE 4: 139:271459  
REFERENCE 5: 138:50247  
REFERENCE 6: 136:401925  
REFERENCE 7: 136:335278  
REFERENCE 8: 136:112696  
REFERENCE 9: 135:358086  
REFERENCE 10: 135:304063

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:50:36 ON 05 SEP 2004

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FILE COVERS 1907 - 5 Sep 2004 VOL 141 ISS 11  
FILE LAST UPDATED: 3 Sep 2004 (20040903/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L27 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:71881 HCAPLUS

DN 136:112696

ED Entered STN: 25 Jan 2002

TI Use of 2-methylene-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D3 to increase bone strength and for the treatment of skin disease, cancer, and bone disease

IN Deluca, Hector F.; Smith, Connie M.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-59

CC 1-12 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005823	A2	20020124	WO 2001-US21706	20010710
	WO 2002005823	A3	20020523		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,				
	HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,				
	LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,				
	RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,				
	YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
	BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1301189	A2	20030416	EP 2001-957115	20010710
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001012454	A	20030729	BR 2001-12454	20010710
	JP 2004505022	T2	20040219	JP 2002-511755	20010710
	US 2004068129	A1	20040408	US 2003-673629	20030929
PRAI	US 2000-616164	A	20000714		
	WO 2001-US21706	W	20010710		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002005823	ICM	A61K031-59
JP 2004505022	FTERM	4C086/AA01; 4C086/AA02; 4C086/DA16; 4C086/GA16; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA89; 4C086/ZA96; 4C086/ZA97; 4C086/ZB26
US 2004068129	ECLA	A61K007/48C4D

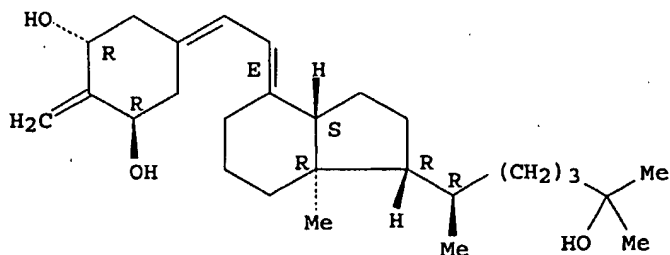
AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1 $\alpha$ ,25-dihydroxyvitamin D3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

ST methylenenordihydroxyvitamin D3 bone strength; cancer psoriasis bone disease methylenenordihydroxyvitamin D3; skin disease osteoporosis methylenenordihydroxyvitamin D3; hip knee replacement methylenenordihydroxyvitamin D3

- IT Animal cell line  
(HL-60; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Mineral elements, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(bone; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Biological transport  
(calcium; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Intestine, neoplasm  
(colon, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(colon; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Cell differentiation  
(inducers; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(leukemia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(low bone turnover osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(mammary gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Monocyte  
Osteomalacia  
Psoriasis  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Vitamin D receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone  
(minerals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Mammary gland  
Prostate gland  
(neoplasm, inhibitors; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(oral; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone, disease  
(osteopenia; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(parenterals; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(postmenopausal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Myelocyte  
(promyelocyte; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Antitumor agents  
(prostate gland; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)

- IT Bone, disease  
(renal osteodystrophy; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Aging, animal  
(senile osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Steroids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(steroid-induced osteoporosis; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Bone  
(strength; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Osteoporosis  
(therapeutic agents; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(topical; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT Drug delivery systems  
(transdermal; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 32222-06-3, 1 $\alpha$ ,25-Dihydroxyvitamin D3 213319-29-0  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 213250-70-5  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 7440-70-2, Calcium, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(transport; methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- IT 213319-29-0  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
- RN 213319-29-0 HCAPLUS
- CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 $\alpha$ ,3 $\beta$ ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



- IT 213250-70-5  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methylenenordihydroxyvitamin D3 to increase bone strength and for



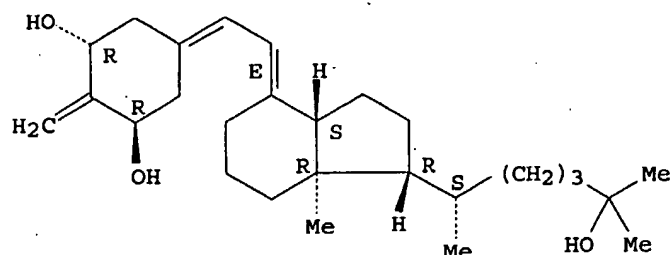
treatment of skin disease, cancer, and bone disease)

RN 213250-70-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,  
(1 $\alpha$ ,3 $\beta$ ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> s 128 not 127

L30 21 L28 NOT L27

=> d bib abs hitstr retable tot

L30 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:522177 HCAPLUS

TI Model of three-dimensional structure of VDR bound with Vitamin D3 analogs substituted at carbon-2

AU Sicinska, Wanda; Rotkiewicz, Piotr; DeLuca, Hector F.

CS Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA

SO Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 107-110

CODEN: JSBBEZ; ISSN: 0960-0760

PB : Elsevier Science Ltd.

DT Journal

LA English

AB All Vitamin D analogs possessing the A ring modified at C-2 and showing calcemic activities nest themselves in the VDR binding pocket, oriented towards Tyr 143. Such topol. resembles the position of the Vitamin D hormone in hVDRmt [Proc. Natl. Acad. Sci. U.S.A. 98 (2001) 5491]. Conversely, inactive 2 $\beta$ -methyl-19-nor-analogs anchor the receptor cavity in a distinguishably different manner, namely by their side chain. Moreover, these inactive vitamins have a different conformation around C(6)-C(7) bond. Topol. of modeled complexes suggests that a Vitamin D analog will be biol. active if its intercylic 5,7-diene moiety assumes parallel position to tryptophan aromatic rings; such orientation allows for creating  $\pi$ - $\pi$  interactions. The broad comparison of calcemic activities of the analogs, and their interactions with VDR, revealed that specific hydrophobic contacts are involved in bone calcium mobilization (BCM). These contacts occur between 21-Me group and a few amino acids (V296, L305 and L309), conserved in the nuclear receptor superfamily. In the inactive 2 $\beta$ -methyl-19-nor analogs such contacts do not exist. We speculate that two hydrophobic receptor patches, being in close contact with ligand Me groups, might influence interaction with co-modulators involved in calcium homeostasis.

IT 213250-70-5 213319-29-0

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(model of three-dimensional structure of VDR bound with Vitamin D3